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Abstract

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Grant Number: 1R29AI036871-01A2
PI Name: WALTER, MARK R.
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PI Title: ASSOCIATE PROFESSOR
Project Title: STRUCTURAL STUDIES OF INTERFERON GAMMA RECEPTOR COMPLEX

Abstract: DESCRIPTION: The goal of the proposal is to understand the structural basis for the specific recognition of cytokines by their receptors. The crystallographic studies of interferon- γ (IFN- γ) and its complexes with a neutralizing Fab fragment as well as with the extracellular fragments of the two recombinant human interferon- γ receptors are in progress. Comparison of the atomic coordinates of all forms of IFN- γ will elucidate the conformational changes that occur upon binding to the receptor. Understanding the structural recognition mechanisms that induce the anti-viral and cytostatic properties of IFN- γ is critical for designing molecules which modulate its activity. Attempts will be made to use the structural results to design and test peptidomimetics or humanized Fab antagonists of IFN- γ . Antagonists of IFN- γ may have therapeutic value in the treatment of autoimmune diseases, chronic inflammation and allograft rejection. Substantial preliminary data have been presented to suggest that the stated goals are feasible.

Thesaurus Terms:

cytokine receptor, interferon gamma, intermolecular interaction, model design /development, molecular shape, protein structure function, receptor binding, structural biology, structural model
conformation, immunoglobulin structure, inhibitor /antagonist
X ray crystallography, crystallization, protein purification, recombinant protein

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